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Does excessive memory load attenuate activation in the prefrontal cortex? Load-dependent processing in single and dual tasks: functional magnetic resonance imaging study

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Abstract

Functional magnetic resonance imaging was used to investigate the relationship between cortical activation and memory load in dual tasks. An *n*-back task at four levels of difficulty was used with auditory–verbal and visual–nonverbal material, performed separately as single tasks and simultaneously as dual tasks. With reference to single tasks, activation in the prefrontal cortex (PFC) commonly increases with incremental memory load, whereas for dual tasks it has been hypothesized previously that activity in the PFC decreases in the face of excessive processing demands, i.e., if the capacity of the working memory's central executive system is exceeded. However, our results show that during both single and dual tasks, prefrontal activation increases continuously as a function of memory load. An increase of prefrontal activation was observed in the dual tasks even though processing demands were excessive in the case of the most difficult condition, as indicated by behavioral accuracy measures. The hypothesis concerning the decrease in prefrontal activation could not be supported and was discussed in terms of motivation factors. Similar changes in load-dependent activation were observed in two other regions outside the PFC, namely in the precentral gyrus and the superior parietal lobule. The results suggest that excessive processing demands in dual tasks are not necessarily accompanied by a diminution in cortical activity.
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Introduction

Working memory (WM) refers to an on-line information processing system and implies temporary storage and transfer of information in the service of higher order cognitive functions such as language comprehension, planning, and problem solving. According to Baddeley (1986), WM consists of several components and supports active maintenance of information as well as executive control processes. A central executive system (CES) is considered responsible for the control and the transfer of information from and to the verbal and spatial "slave systems" (phonological loop and visuospatial sketchpad) and is seen as being involved in the allocation and coordination of attentional resources. It is assumed that the capacity of the CES is limited.

Various functional imaging studies with positron emission tomography and functional magnetic resonance imaging (fMRI) provided strong evidence of prefrontal cortex (PFC) involvement in a wide variety of tasks related to working memory (for a review, see D'Esposito et al., 1998, or Fletcher and Henson, 2001). It has been suggested that there is a functional specialization within the PFC in relation to WM regarding the type of processes operating on the memoranda. While the ventrolateral PFC (VLPFC; BA 44/

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5/47) is concerned with active maintenance and updating f information, i.e., with tasks conducted by the phonolog- al loop and the visuospatial sketchpad, the dorsolateral FC (DLPFC; BA 9/46) is seen as mediating active manip- lation and monitoring, i.e., executive control (Petrides, 994; Owen et al., 1998; Fletcher and Henson, 2001). How- ver, activation of additional brain regions has commonly een observed during the performance of WM tasks (e.g., osterior parietal cortex, as well as premotor and supple- entary motor regions), suggesting that WM functions are ubserved by multiple brain regions.

The present study focused on the role of WM, especially oncerning executive control processes and their neural epresentations.

The dual-task paradigm has been widely used as an ffective experimental tool to investigate such executive ontrol processes as well as their limits, since the concurrent erformance of two tasks requires distribution of attentional esources to different simultaneous processes, which is one f the main functions attributed to the CES.

Lesion studies have shown that patients with prefrontal amage are generally impaired in performing dual tasks hile performance in single tasks is relatively preserved Baddeley et al., 1991, 1997; McDowell et al., 1997).

On the basis of functional imaging data, D'Esposito et al. 1995) suggested that the PFC is critical for the CES. They ompared single-task performance of two non-WM tasks ith a concurrent performance of both tasks, which was xpected to engage WM and, especially, the CES. Activa- on of the DLPFC occurred only during the dual-task con- ition and not when either task was performed alone. These ndings have been attributed to the supplementary engage- ent of WM in this condition and were taken as evidence or a neural basis of the CES in the PFC. This interpretation consistent with the idea that the simultaneous perfor- ance of two tasks compared to single-task performance equires additional mental resources, which could be dopted by novel areas specialized for dual-task-specific rocesses not required in either single task, such as task oordination or shifting attention.

However, several studies failed to elicit such a "surplus" ctivation in the DLPFC during dual tasks compared to ngle tasks (Klingberg, 1998; Goldberg et al., 1998, Ad- ock et al., 2000; Bunge et al., 2000). In all of these studies, he single tasks per se engaged WM and the DLPFC was ready activated under these single-task conditions. There evidence that if the DLPFC is already activated in the ngle tasks, activation does not increase further during the erformance of a secondary task. For example, Klingberg 1998) did not find additional activation in the PFC during ual tasks, relative to the activation during the single tasks. hus, he could not observe a separate cortical area that ould be associated with a specific cognitive process, taking lace only during dual tasks. More recent studies have also hown no evidence for an additionally activated site for a ossible CES expressed in the recruitment of novel prefron-

tal (or any other) regions during dual-task performance relative to the performance in the single tasks. Rather, dual-task processing was associated with a stronger and more extensive magnitude of activation in regions activated by either single task (Adcock et al., 2000; Bunge et al., 2000). Therefore, additional resources required for the per- formance of dual tasks seem to be reflected as enhanced activation in the same brain regions that subserve perfor- mance in either single task. Finally, Goldberg et al. (1998) reported even a decrease of PFC activation during their dual-task condition compared to the activation pattern under their single-task conditions. In consideration of these re- sults, D'Esposito (2001) concluded that "under dual task conditions activation in the PFC would increase as a result of greater demands on processing, up to some level of asymptote, before attenuating," i.e., if the capacity of the CES is exceeded, cortical activity in the PFC may decrease.

Additional theoretical considerations concerning these results were made by Goldberg et al. (1998). They consid- ered capacity limits of the CES as well as the concept of cognitive workload, a concept characterized as the differ- ence between the expected and the actual performance of a task due to an increase in task difficulty (Gopher and Donchin, 1986). An increase in cognitive workload may be associated with a decrement of performance, and WM should be especially susceptible to manipulations of work- load, since WM is thought to be of limited capacity. Thus, Goldberg and colleagues suppose that the impact of exces- sive workload on WM could lead to an attenuation of prefrontal activation, which could indicate a breakdown in neural networks. Because of the substantial increase of cognitive workload under dual-task conditions, the capacity limits of the CES are quite quickly reached, leading to the reported decrements of accuracy together with decreases in fMRI signal intensity in some cortical sites that are assumed to be related to the CES (mainly in the DLPFC).

Another slightly different explanation goes back to a recent fMRI study reported by Just et al. (2001) in which activations in dual and single tasks were compared in dif- ferent cortical areas. They hypothesized that if two tasks compete for a common resource pool, i.e., for the same brain regions, there should be less activation in those re- gions during the concurrent performance of the two tasks than the sum of activation under the two single-task condi- tions. However, concerning the PFC, Just et al. (2001) reported similar activation for the dual-task condition com- pared with the summed activation of both single tasks. But even though both single tasks activated the PFC, activation in that area was minimal, leaving the question open of whether dual-task activation would decrease further if the PFC was more substantially activated.

Thus, it seems that activation in the PFC during the concurrent performance of two tasks can exceed the activa- tion during the single-task conditions, as long as the single tasks do not compete for the same resources, or as long as

memory load in the single tasks only induces minimal PFC activation.

A crucial question is now whether the enhanced prefrontal activation during dual tasks in the studies cited above was actually due to an increase of WM demands or rather reflected an unspecific increase in "mental effort" or arousal, due to greater task difficulty. This question of task difficulty and its confounding with WM load was directly addressed in a study by Barch et al. (1997). They systematically varied cognitive workload and task difficulty by increasing task difficulty independent of WM demands by using degraded stimuli to enhance task difficulty and delay variation to enhance WM load. In fact, they found a double dissociation between regions recruited in WM tasks (DLPFC, Broca's area, and parietal cortex) and those recruited in task difficulty (primarily anterior cingulate). Thus, the DLPFC seems indeed to be involved in WM processing. Other imaging studies supply further evidence that the prefrontal region is quantitatively more activated if the WM load is increased (Braver et al., 1997; Cohen et al., 1997; Jonides et al., 1997; Owen et al., 1996; Petrides et al., 1993a, 1993b; Schumacher et al., 1996; Smith and Jonides, 1997). However, the processing demands in these studies, expressed in accuracy, never fell below 75%, which could indicate that the subjects never reached the limit of their processing capacity. Therefore, it is not clear whether activation would still increase in such a case.

The present study investigated cortical activation with functional MRI during the systematic variation of memory load both in single *and* in dual tasks. To this end we used a variation of the *n*-back paradigm adapted from Gevins and Cutillo (1993) at four levels of difficulty with auditory–verbal and visual–nonverbal material (see Fig. 1). This task generates a specific response pattern in behavioral performance as well as in the fMRI signal and has reliably produced activation in WM-related cortical regions (Braver et al., 1997; Cohen et al., 1997; Jonides et al., 1997). The *n*-back paradigm requires a continuous monitoring of sequentially presented stimuli, and subjects must answer positively whenever the current stimulus matches the stimulus occurring *n* positions back in the sequence. The task combines maintenance as well as active manipulation, i.e., executive processes, because of the necessity to continuously encode, update, and discard the information held in WM with the presentation of each new stimulus. The value of *n* is regarded as proportional to memory load (Braver et al., 1997).

On the basis of earlier findings several hypotheses were tested.

First, for the single tasks it was predicted that cortical activity increases in proportion to the WM demands, i.e., we expect a linear relationship between activity and WM load, especially in the PFC (Braver et al., 1997; Cohen et al., 1997; Jonides et al., 1997; Owen et al., 1996; Petrides et al., 1993a, 1993b; Schumacher et al., 1996; Smith and Jonides, 1997). The pattern of activation should not differ quantita-

tively and qualitatively in most areas (i.e., no increasing activation and no recruitment of additional areas with increasing WM demands) with the exception of the DLPFC (BA 46/9) and Broca's area (BA 44/45) where, by comparing the 1-back with the 2-back condition, we expect an increase in cortical activation due to novel task demands (updating and rehearsal).

Second, for the dual tasks the hypothesis formulated by D'Esposito (2001; see above) was tested: initially, activation in the PFC should gradually increase due to the augmentation of processing demands on the WM; but, when processing demands reach a level where the subject is unable to perform the task with an accuracy above chance level, we predict an attenuation of prefrontal activation.

Third, comparing the activation pattern in the summed single tasks with the corresponding dual tasks, it is predicted that the greater the sum of the activation with increasing memory load during the single tasks in a given area (here, in the DLPFC), the smaller the portion of activation resulting from the dual tasks in comparison with the sum of activation in the single tasks (Just et al., 2001). Thus, there should be an interaction between the sum of activations in the single tasks and those of the corresponding dual tasks with increasing memory load, i.e., in the 1-back condition, the sum of the activations of the two single tasks should be smaller than the activation in the corresponding dual task, whereas in the 3-back condition, the summed activations of the two single tasks should exceed the activation of the dual task.

Materials and methods

Subjects

Six subjects (three female, three male; age range 24 to 27 years; mean 25.3) participated in this study. All were assessed as right-handed (Oldfield, 1971) with no seeing, hearing, or neurological disorders and normal structured MRI scans. All participants gave written informed consent according to a protocol approved by the local ethics committee. All subjects were given identical practice with the task and were scanned only after reaching a criterion level of performance (>75% accuracy in the 2-back single task).

Task design

Materials

The *n*-back paradigm was used at four levels of difficulty with auditory–verbal and visual–nonverbal material, constructed as single tasks as well as dual tasks.

The auditory–verbal material consisted of 10 consonants (b, c, d, g, h, k, p, q, t, and w), which were spoken by two males and two females. The voice was varied in order to prevent a low-level auditory-matching strategy. The visual–nonverbal stimuli were drawn from a set of 10 abstract
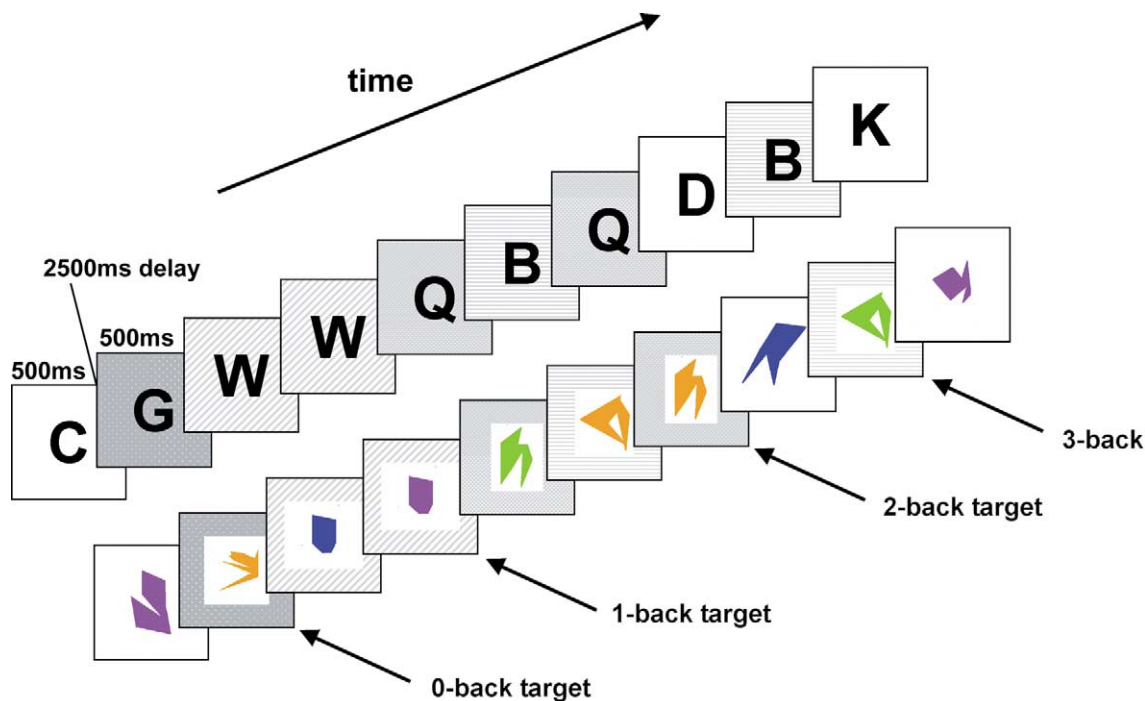
Fig. 1. The four memory conditions for the sequential *n*-back task. Under the 0-back condition, the task was to respond to a prespecified target (e.g., "G"), whereas under the other conditions, a response was required whenever the current stimulus matched the stimulus 1, 2, or 3 positions back in the sequence. Thus, WM load increased gradually from the 0-back to the 3-back condition. The task was performed as single task with auditory–verbal and visual–nonverbal material, as well as a dual task, where the attention had to be divided between two tasks presented simultaneously in either modality.

random shapes (Attneave and Arnoult, 1956) with low association value, i.e., which were difficult to verbalize (Vanderplas and Garvin, 1959; numbers 14, 15, 17, 18, 20, 22, 23, and 27 of the 8-point shapes, as well as numbers 20 and 24 of the 12-point shapes). The shapes were stained with four different colors (blue, green, orange, magenta) which were varied in order to prevent a low-level visual-matching strategy.

The stimulus material was carefully chosen on the basis of preexperiments (not described in this paper) for the purpose of adapting the difficulty level between input modalities (auditory–verbal and visual–nonverbal) in order to make sure that both corresponding single tasks required similar working memory demands under the dual-task conditions. Successful adaptation of the difficulty level was achieved as the behavioral data (accuracy and reaction times) in the corresponding tasks were comparable in both modalities (e.g., same accuracy and same reaction times in the 2-back condition in the visual–nonverbal and the auditory–verbal tasks).

For each difficulty level and modality, computerized lists of 64 stimuli were constructed for both single and dual tasks, whereas the lists of the dual tasks consisted of one list for each modality. For the single tasks, each list consisted of 16 targets and 48 nontargets and for the dual tasks of 8 targets and 56 nontargets in each modality, respectively. Corresponding to the later fMRI requirements, the lists were divided into eight sequences with 2 targets and 6 nontargets

for the single tasks and 1 target and 7 nontargets for each modality for the dual tasks, respectively.

Under the 0-back condition, the target was a single prespecified stimulus. Under the 1-back condition, the target was any stimulus identical to the one immediately preceeding it (one trial back). Under the 2-back and 3-back conditions, the target was any stimulus identical to the one presented two or three trials back, respectively (see Fig. 1).

Targets and nontargets were determined pseudorandomly, i.e., varying the position of the targets in each sequence randomly in the single tasks and pseudorandomly in the dual tasks, i.e., to make sure that the two targets were never set at the same position in both modalities. In addition, the rate of occurrence of each stimulus was held constant over the whole list. Color and voice were varied randomly.

Procedure

Stimulus presentation and response recording were controlled by a Macintosh computer using PsyScope software (Cohen et al., 1993). Visual stimuli were projected centrally onto a translucent screen, which was visible for the subjects through a mirror mounted above the head coil. Auditory stimuli were played through headphones. The volume was adjusted to be comfortably audible. The subjects were instructed to respond to each target by pressing a pneumatic squeeze ball using their dominant hand.

While being scanned, the subjects had to alternate be-

ween two different task conditions (two different *n*-back
tasks) every 24 s, eight times, in a total of 6.4 min. Accord-
ing to the required task contrasts all subjects completed
seven different task alternations. All task alternations were
trained beforehand in a practice session. Alternation was
automatically triggered by the computer. In order to analyze
only data with steady-state task performance (and steady-
state MRI signal) all task alternation started with an addi-
tional constructed warm-up task (identical to one of the task
alternations). Data from this warm-up task were discarded
from further data analysis.

The order of the task alternations was varied randomly
for each subject. Four task alternations consisted of single-
task combinations (auditory 1-back vs 2-back, auditory
2-back vs 3-back, visual 0-back vs 2-back, visual 1-back vs
3-back) and three task alternations consisted of dual-task
combinations (0-back vs 1-back, 0-back vs 2-back, 1-back
vs 3-back). Stimuli were presented sequentially for 500 ms
with a 2500-ms interstimulus interval (ISI). Under the dual-
task conditions the auditory and visual stimuli were pre-
sented at the same time. Task alternations were indicated
centrally on the screen, presenting specified instruction
signs (0 for the 0-back task, Roman numbers for the other
tasks (I, II, III), respectively) during the ISI before each
alternation (2000-ms duration, 250-ms ISI before and after
the instruction sign).

Subject performance during scanning was monitored in
terms of reaction time and accuracy (number of target letters
identified correctly). In addition, subjects answered a ques-
tionnaire in which they rated the subjectively experienced
demands of each task on a five-point scale from small to
excessive demands.

Data acquisition

Imaging was performed as previously described (Nirkko
et al., 2001). In short, we used a 1.5-T whole-body MRI
scanner (Magnetom Vision, Siemens Medical Systems, Er-
langen, Germany) with its standard whole-body gradient
system and circularly polarized head coil. To restrain head
motion in all directions, the subjects were fixed with both
the standard lateral pads and a smooth U-shaped plastic
dental plate functioning as an improved bite bar. After
shimming, whole brain fMRI was performed with a blood
oxygenation level dependent (BOLD) echo-planar imaging
(EPI) sequence (matrix $128 \times 128 \times 30$ slices $\times$ 68
measurements, resulting in $1.56 \times 1.56 \times 4$ mm $\times$ TR 6 s;
TE 82 ms). Phase-encoding direction was anteroposterior,
thus preserving brain symmetry. Slice angulation was par-
allel to a line connecting the base of the genu corpori callosi
and the confluens sinuum, resulting in an angle of about
20–30° with respect to the bicommissural (AC–PC) line
(Nirkko et al., 2001). Between fMRI experiments, standard-
ized sets of high-resolution structural images were acquired

Data analysis

Behavioral data

Behavioral data (accuracy and reaction times) were an-
alyzed in order to evaluate the subjects' compliance with the
task along with the effectiveness of the manipulation of
WM load in single and dual tasks and further, to control
differences in performance across modality (auditory–ver-
bal vs visual–nonverbal). The subjects' performance was
evaluated using two-way repeated-measures ANOVA with
condition (single vs dual task) and load (1-back to 3-back)
as within-subjects factors. Differences in performance
across modality (auditory–verbal vs visual–nonverbal) were
analyzed using a two-way repeated-measures ANOVA with
modality and load (1-back and 2-back) as within-subjects
factors.

Post hoc tests for significant main effects and contrasts
for significant interactions were performed throughout and
were corrected for multiple comparisons (Bonferroni cor-
rection).

fMRI evaluation

We used a methodology of fMRI evaluation respecting
interindividual cortical variability and allowing direct sta-
tistical comparison between experimental tasks and brain
regions. To compare the amount of activation in a given
area across experimental tasks, anatomical defined regions
of interest (ROI) were drawn for each subject using the
parcellation scheme described by Rademacher et al. (1992).
In order to examine not just the location of activation but
also how the experimental tasks affected the magnitude of
the activation in each of these regions, it was important to
use an a priori, independent method of defining the ROIs
(Nirkko et al., 2001; Michael et al., 2001). This method uses
limiting sulci as anatomical landmarks to segment cortical
regions. The schematic drawing in the center of Fig. 3
displays the set of ROIs that were defined.

Specifically designed software was used to delineate the
ROIs manually on each EPI slice of each subject (Nirkko,
2000). Delineation was done by two staff research assistants
after extensive training in the Rademacher parcellation
scheme. To optimize reliability we created a standard ana-
tomical atlas using the EPI images of one of our subjects as
an explicit guide to the delineation of individual sulci fol-
lowing the suggestions of Rademacher et al. (1992), Cavi-
ness et al. (1996), Ono et al. (1990), and Damasio (1995).
The interrater reliability of this ROI-defining procedure
between the two trained staff members was evaluated for all
ROIs in one task for two subjects. The reliability measure
was obtained by calculating correlations between the two
raters based on percentage signal change relative to the
control task average. An interrater reliability measure of $r =$
0.93 in one subject and of $r = 0.82$ in the other subject
reflects a high degree of reliability in the ROI-defining
procedure.

Seven volumes of interest (VOI; each composed of sev-

esponding ROIs in several slices) of the lateral and medial erebral surface were specified in each hemisphere (see chematic drawing in the center of Fig. 3).

Laterally, the DLPFC was defined as the middle frontal yrus (F2; BA 6,8,9, and 46) with the exception of the osterior-most part (frontal eye fields) to exclude activation elated to eye movements. The inferior frontal VOI included 3o and F3t (BA 44 and 45). The temporal VOI comprised he superior (T1a and T1p) and middle (T2a and T2p) emporal gyri (BA 21 and 37). These gyri were combined ito one VOI because previous studies of other cognitive rocesses (e.g., language) have often found activation cenered in the superior temporal sulcus between them (Keller al., 2001; Michael et al., 2001). The parietal VOI consted of the superior parietal lobule (BA 21 and 37). The recentral VOI corresponded to the precentral gyrus (PRG; A 4). Medially, the supplementary motor area VOI consted of parcellation unit SMC (BA 6) and finally, the nterior cingulate VOI was CGa (BA 24).

No maximum z score values or counts of significant ixels were used for quantitative evaluation since both staistical z values and thresholded pixel counts are highly onlinear and depend not only on the signal increase, but so on the number of measurements and the amount of oise and thus invalidate averaging of interindividual, inertask, and even interregion comparisons: for instance, a igher z score can result from a region with a smaller signal hange, but less noise. This is evident from the formula to alculate z scores, but in essence also holds for other staistical values like t tests. Using the formula for the z score or independent samples,

$$z = \frac{m_1 - m_0}{\sqrt{\dfrac{V_1}{n_1} + \dfrac{V_0}{n_0}}},$$

here m_1 and m_0 are the mean values for activation and rest, $_1$ and V_0 are the variances, and n_1 and n_0 are the number f respective samples, and given the nonlinear characterisics of the variance calculation itself, it can be seen that the core is nonlinearly and inversely related to the variances (a easure of the noise contained in the data) and the number f samples and that the z score of the average (or sum) of wo values does not equal the average (or sum) of the two scores. Moreover, selecting "activated pixels" above a ertain threshold is a nonlinear operation by definition. While this is valid and very useful as an endpoint for isualization of significant areas, using activated pixels as a eparting point for further analysis is highly problematic ecause of these relationships: in particular, averaging or therwise evaluating counts of activated pixels for comparion between tasks, as in comparing whether the sum of the ctivation of two tasks exceeds the activation of another sk, is mathematically and statistically invalid: as a realistic xample, assuming a homogenously activating region of 00 independent pixels, a standard deviation of 2%, 30

measurements for activation and 30 for baseline, and a z score threshold of 2.0, the number of activated pixels in that region will remain 0 between a signal change of 0% and 0.8, then steeply rise from 8 pixels at 0.9% signal change to 96 pixels at 1.2% signal change, above which all 100 pixels will activate. This demonstrates the highly nonlinear behavior of activated pixel counts (higher z score thresholds and larger number of measurements will even increase the nonlinearity). Now if, in this example, the relation between two component tasks and a combined "additive task" were to be assessed, and this region activated 0.5% in each component task and 1.0% in the additive task, resulting pixel counts will be 0 for the components and 36 for the additive task, resulting in the interpretation that the additive task with 36 activated pixels demands much more than the sum of the component tasks with 0 pixels each, i.e., reveals a new region specific to the combination of the two tasks, but not to the component tasks themselves. Conversely, if each component would activate 1.2% and the additive task 2.4%, pixel counts would be 96 for the components and 100 for the additive task, resulting in the interpretation that the additive task is not additive at all, but demands no more than each component task. In both cases, the interpretation is wrong because statistical end results were used in an invalid way as a starting point for further calculations. The correct interpretation results from using the mean values of the signal changes themselves, which in both cases shows that the additive task activation correspond to the sum of each component task, whether it is $0.5 + 0.5 = 1.0$ or $1.2 + 1.2 = 2.4$. With these signal change values as starting point, further calculations and statistical tests can be done (despite being aware of the possibility of a mild nonlinearity of the BOLD response itself (Friston et al., 2000), in practice probably only significant at very high activation levels). With thresholded pixel counts, or signal changes based on activated pixels only, instead of unselected pixels, the calculations are strongly false and mathematically invalid in the first place. To avoid these problems, we used the percentage signal change relative to the control task average, which in each VOI from all subjects was subjected to the typical statistical procedure, i.e., testing the null hypothesis of no change by calculation of z scores. In addition, the resulting percentage signal change (between activation and control task), as determined for each VOI, allowed for averaging between subjects and further statistical comparison between tasks and regions. Minimal statistical significance was set at the conventional $P < 0.05$ (corrected for multiple comparisons with the Bonferroni correction); higher significance levels are labeled in the corresponding table legend. From the resulting percentage signal changes in the seven realized task alternations, it was possible to calculate the percentage signal change of other contrasts. For example, from the task alternations visual 0-back vs 2-back and 1-back vs 2-back, the contrast visual 0-back vs 1-back could be derived, due to the fact that the two primal
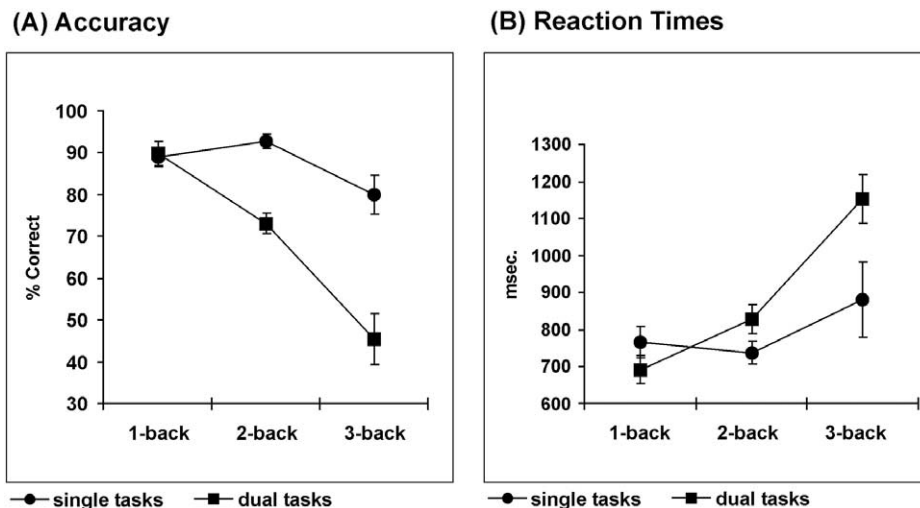
(A) Accuracy

(B) Reaction Times

g. 2. Means and standard errors of the behavioral data (accuracy (A); reaction time (B)) during the fMRI session as a function of task load (from 1-back 3-back).

process-specific" theory says that the DLPFC is involved processes such as monitoring and higher-level planning d not sensitive for different types of information (Fletcher d Henson, 2001; D'Esposito and Postle, 1999; Petrides, 994, 1995), we assumed that there are no differences in DLPFC activation across modality (auditory–verbal vs viual–nonverbal). In that case, the results of the realized ontrasts in auditory–verbal and visual–nonverbal single asks could be summed up in one line of single tasks with ncreasing load (1-back to 3-back task as activation tasks ith the 0-back task as control). To control the differences the percentage signal change across modality (auditory– erbal vs visual–nonverbal), we compared the contrast -back vs 2-back, which was realized under both the audiory–verbal and the visual–nonverbal conditions, using a wo-way repeated-measures ANOVA (SPSS for Windows, elease 10.0) with hemisphere and modality as withinubjects factors for each VOI.

To compare signal changes in single and dual tasks, as ell as to test a possible interaction between these condions, repeated-measures ANOVAs were performed, with ondition (single vs dual tasks), load (1-back to 3-back), and emisphere (left vs right) as within factors for each VOI.

Additionally, to directly test our hypotheses concerning e load-dependent changes in the percentage signal change eparately for single and dual tasks, repeated-measures ANOVAs were performed, with load (1-back to 3-back) and emisphere (left vs right) as within factors for each VOI.

In analogy to Just et al. (2001), the comparison of the ctivation pattern of the dual tasks with the sum of the orresponding single tasks was analyzed using a three-way epeated-measures ANOVA with condition (sum of the sinle tasks vs dual tasks), load (1-back to 3-back), and hemiphere (left vs right) as within-subjects factors for each OI.

Significant main effects and interactions were followed

by post hoc tests and contrasts and were corrected for multiple comparisons (Bonferroni correction).

Results

Behavioral data for single and dual tasks

A two-way repeated ANOVA for both behavioral measures, i.e., the accuracy and the reaction time (RT), indicated a significant main effect of load, i.e., 1-back to 3-back tasks (accuracy: $F(2,5) = 13.24$; $P = 0.006$; RT: $F(2,5) = 21.09$; $P = 0.002$), with a significant interaction between condition (single vs dual tasks) and load (1-back to 3-back) for accuracy ($F(2,5) = 6.73$; $P = 0.029$). The data in Fig. 2 show that, as anticipated, increasing processing load made the task more difficult, as reflected in both the response times and the accuracies. Post hoc tests only reached significance in the dual tasks: there was a significant difference between the 1-back and the 3-back task in accuracy ($P = 0.000$), as well as between the 1-back and the 2-back task in RT ($P = 0.000$). The interaction between condition and load revealed that, concerning accuracy, the observed load effect was more substantial in the dual tasks than in the single tasks. The accuracy as a function of memory load declined less in the single tasks than in the dual tasks. In the single tasks, accuracy decreased from 89% (SEM: 4.67) in the 1-back task to 80% (SEM: 9.13) in the 3-back task, whereas in the dual tasks it declined from 90% (SEM: 5.74) in the 1-back task to 45% (SEM: 12.08) in the 3-back task. In this dual 3-back task, none of the subjects showed a performance which differed significantly from chance level.

According to contrasts, only the performance in the dual 2-back tasks differed significantly from the performance in the corresponding single tasks ($t(5,5) = 3.41$; $P = 0.028$).

Table 1
Means and standard errors (in parentheses) for seven volumes of interest (VOI)

VOI	Single tasks			Dual tasks		
	1-back	2-back	3-back	1-back	2-back	3-back
Left DLPFC	−0.15** (0.16)	0.04 (0.18)	0.49*** (0.08)	0.11 (0.03)	0.21*** (0.08)	0.41*** (0.08)
Right DLPFC	−0.11 (0.10)	0.06 (0.09)	0.43*** (0.10)	0.15* (0.04)	0.17* (0.07)	0.38*** (0.08)
Left inferior frontal gyrus	0.09 (0.10)	0.18 (0.14)	0.43*** (0.16)	0.19** (0.07)	0.10 (0.06)	0.39*** (0.10)
Right inferior frontal gyrus	0.00 (0.09)	0.07 (0.08)	0.20* (0.15)	0.10* (0.07)	0.03 (0.08)	0.20*** (0.10)
Left superior parietal lobule	0.14 (0.16)	0.43*** (0.10)	0.45*** (0.18)	0.25*** (0.07)	0.40*** (0.08)	0.51*** (0.07)
Right superior parietal lobule	0.21 (0.14)	0.48*** (0.10)	0.57*** (0.18)	0.28*** (0.08)	0.38*** (0.10)	0.54*** (0.11)
Left precentral gyrus	0.02 (0.09)	0.32 (0.10)	0.70*** (0.14)	0.26* (0.05)	0.28** (0.08)	0.49*** (0.18)
Right precentral gyrus	−0.11* (0.10)	0.08 (0.12)	0.40*** (0.07)	0.16 (0.05)	0.13 (0.07)	0.28** (0.10)
Left temporal	−0.08 (0.14)	0.01 (0.08)	0.12 (0.08)	0.02 (0.07)	−0.10 (0.04)	0.02 (0.05)
Right temporal	−0.11 (0.14)	−0.05 (0.11)	−0.11 (0.07)	0.00 (0.07)	−0.19** (0.05)	−0.11** (0.08)
Left anterior cingulate gyrus	−0.15 (0.10)	−0.02 (0.07)	0.17 (0.08)	0.06 (0.06)	0.06 (0.08)	0.08 (0.10)
Right anterior cingulate gyrus	0.03 (0.17)	0.11 (0.11)	0.08 (0.06)	0.05 (0.06)	−0.09 (0.04)	0.07 (0.13)
Left supplementary motor area	−0.04 (0.19)	0.19 (0.17)	0.25*** (0.19)	0.04 (0.07)	0.18 (0.16)	0.19* (0.15)
Right supplementary motor area	0.16 (0.33)	0.32 (0.31)	−0.03 (0.10)	−0.04 (0.04)	−0.20 (0.14)	0.02 (0.11)

Note. Values are given as group average of percentage BOLD signal change with statistical group analysis of fMRI data from VOIs. * $P < 0.05$ ($z > 2.80$); ** $P < 0.01$ ($z > 3.891$); *** $P < 0.001$ ($z > 4.417$); corrected for multiple comparisons (Bonferroni). DLPFC, dorsolateral prefrontal cortex.

formance across input modality of the stimuli (auditory–verbal vs visual–nonverbal), either in accuracy ($F(1,5) = 0.90$; $P = 0.387$) in RT ($F(1,5) = 5.54$; $P = 0.065$).

Imaging data

Generic brain activation

The average of percentage BOLD signal change and significance levels for the volumes of interest are given in Table 1. At the highest task load (3-back single and dual task), a significant response was observed in a distributed cortical network, comprising bilateral dorsolateral prefrontal cortex (BA 6, 8, 9, and 46), bilateral inferior frontal gyrus (BA 44 and 45), bilateral superior parietal lobule (BA 21 and 37), bilateral precentral gyrus (BA 4), and the left supplementary motor cortex (BA 6).

A significant response during nearly all working memory conditions, both in single and dual tasks, only appeared in the bilateral superior parietal lobule (BA 21 and 37). Additionally, there were two regions producing significant activations during all dual-task conditions, namely the left precentral gyrus (BA 4) and the right DLPFC. In the left DLPFC and the bilateral inferior frontal gyrus, significant

responses were observed in two of three dual-task conditions. None of the explored VOIs exhibited modality effects based on material (auditory–verbal vs visual–nonverbal; see below).

Load-dependent activation changes in both single and dual tasks in the DLPFC

A three-way ANOVA with condition (single vs dual tasks), load (1-back to 3-back), and hemisphere (left vs right) as within factors for each VOI revealed only a significant main effect of load ($F(2,5) = 18.57$; $P = 0.000$), with a significant linear trend ($P = 0.003$), but no interaction between conditions (single vs dual tasks) ($F(2,5) = 2.46$; $P = 0.135$). Post hoc tests showed significant differences in percentage signal change between the 1-back and the 3-back ($P = 0.009$) and between the 2-back and the 3-back conditions, respectively ($P = 0.040$).

Hypothesis I: load-dependent activation changes in single tasks in the DLPFC

As expected, the repeated-measures ANOVA indicated a significant main effect of load in this region ($F(2,5) = 9.82$; $P = 0.004$). The percentage signal change continuously

increased from the 1-back to the 3-back condition (1-back: .13% (SEM: 0.12); 2-back: 0.05% (SEM: 0.13); 3-back: .46% (SEM: 0.08)). The linear trend was significant ($P =$ .016). Post hoc tests showed only a significant difference n percentage signal change between the 1- and the 3-back asks ($P = 0.048$) (Fig. 3).

ypothesis II: load-dependent activation changes in dual asks in the DLPFC

Similar to the single tasks, the repeated-measures NOVA showed a significant main effect of load ($F(2,5) =$ 3.17; $P = 0.002$). The percentage signal change increased nearly from the 1-back to the 3-back condition (1-back: .13% (SEM: 0.02); 2-back: 0.19% (SEM: 0.06); 3-back: .39% (SEM: 0.07)). The linear trend was significant ($P =$ .012). Post hoc tests showed significant differences in ercentage signal change between the 1-back and the 3-back $P = 0.036$), as well as between the 2-back and the 3-back asks ($P = 0.004$).

Hypothesis III: load-dependent activation changes in dual tasks compared with the summed activations of the corresponding single tasks

Since no VOI showed a significant difference in the percentage signal change across modality (see below), the sum of the single tasks was computed as doubled activation of the corresponding single task. A three-way repeated-measures ANOVA with condition (sum of the single tasks vs dual tasks), load (1-back to 3-back), and hemisphere as within-subjects factors showed that the DLPFC produced a significant main effect of load ($F(2,5) = 14.49$; $P = 0.001$) as well as a significant interaction between condition and load ($F(2,5) = 5.55$; $P = 0.024$). The increase of the activation change as a function of task load was more substantial in the single tasks than in the dual tasks (see Fig. 4).

However, the contrasts showed no significant differences between the activation of the sum of single tasks and the activation of the corresponding dual tasks under the 1-back and the 2-back conditions (Fig. 5). Under the 3-back con-
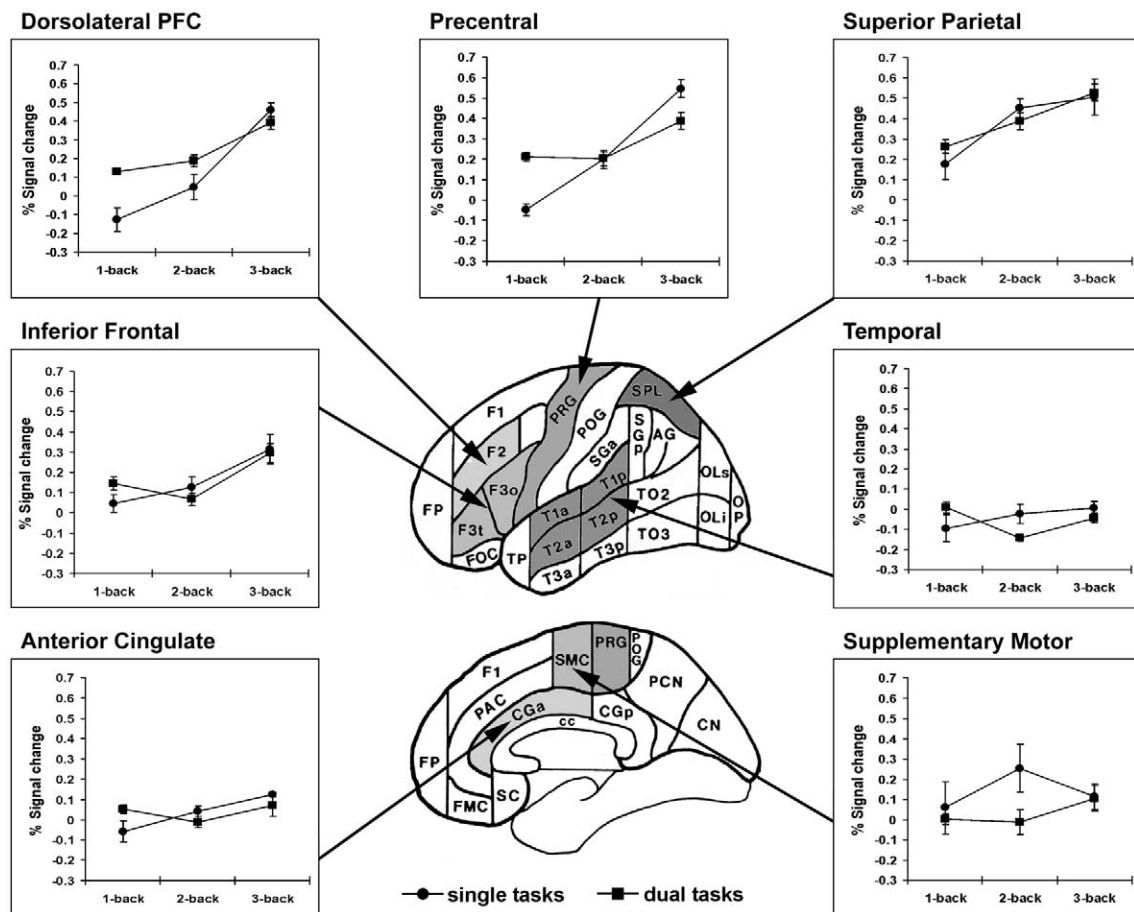

g. 3. The schematic drawing in the center shows the anatomical defined volumes of interest (VOI), adapted from the parcellation scheme described and epicted in Rademacher et al. (1992); laterally, the dorsolateral prefrontal cortex, the inferior frontal gyrus, the precentral gyrus, the superior parietal lobule, d the temporal region; medially, the supplementary motor area and the anterior cingulate gyrus. Each area shaded in gray represents a VOI. The associated aphs depict the amount of activation in the seven given VOIs as a function of memory load (1-back to 3-back tasks, with the 0-back task as control) for th the single and the dual tasks. The amount of activation is defined as group average of percentage BOLD signal change. The error bars represent the
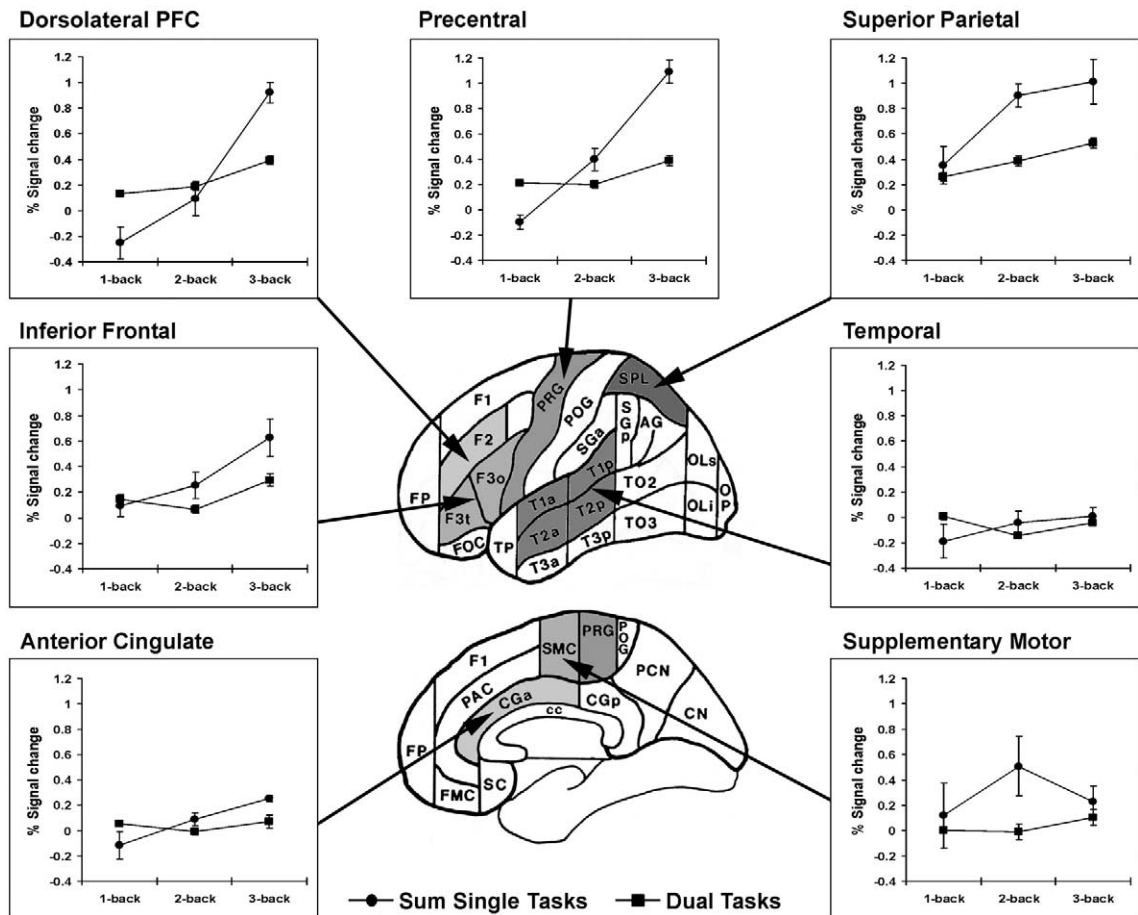
Fig. 4. The schematic drawing in the center shows the anatomical defined volumes of interest (VOI), adapted from the parcellation scheme described and depicted in Rademacher et al. (1992). The associated graphs depict the amount of activation in the seven given VOIs as a function of memory load (1-back [to] 3-back tasks, with the 0-back task as control) for the sum of the single tasks and the corresponding dual tasks. The sum of the activations in the single [ta]sks was computed as doubled activation of the corresponding single task. The error bars represent the standard error of the mean.

[...]tion, the activation of the sum of the single tasks was [te]ndentially stronger than the activation of the dual task (P [=] 0.084). The 3-back dual task produced only 42% as much [a]ctivation as the sum of the two corresponding single tasks.

[O]ther regions with load-dependent signal change

Apart from the DLPFC, two other regions exhibited a [m]ain effect of load, the superior parietal lobule and the [p]recentral gyrus. In both VOIs the percentage signal change [in]creased from the 1-back to the 3-back condition [superior [p]arietal lobule: 0.22% under 1-back (SEM: 0.07), 0.42% [u]nder 2-back (SEM: 0.04), and 0.52% under the 3-back [c]ondition (SEM: 0.10); $F(2,5) = 4.29$; $P = 0.045$; precen-[tr]al gyrus: 0.08% under 1-back (SEM: 0.03), 0.20% under [2]-back (SEM: 0.05) and 0.47% under the 3-back condition [(S]EM: 0.09); $F(2,5) = 18.36$; $P = 0.000$]. The post hoc [te]sts for the superior parietal lobule showed significant [d]ifferences in percentage signal change between the 1-back [an]d the 2-back conditions ($P = 0.042$). The linear trend was [on]ly significant in the precentral gyrus ($P = 0.006$). Fur-[thermore, in addition to the main effect of load, the precen]-

tral gyrus revealed a significant interaction between condi-tion (single vs dual task) and load ($F(2,5) = 7.45$; $P = 0.01$). The increase in the activation change as a function of task load was more substantial in the single tasks than in the dual tasks. The activation in the 1-back dual-task condition tendentially exceeded the activation during the correspond-ing single task ($t(5,5) = -3.10$; $P = 0.085$), but increased less with higher task loads, expressed in a significant smaller dual-task activation under the 3-back condition ($t(5,5) = 3.55$; $P = 0.048$) compared with the activation in the corresponding single task (see Fig. 3).

In a third region, in the inferior frontal gyrus, the acti-vation increased tendentially as a function of load ($F(2,5) = 3.71$; $P = 0.062$). Additionally, this region showed a sig-nificant main effect of hemisphere ($F(1,5) = 49.16$; $P = 0.001$). This hemisphere main effect appeared also in the temporal VOI ($F(1,5) = 10.16$; $P = 0.024$). In both VOIs, the left hemisphere was more activated than the right hemi-sphere. In addition, for the temporal VOI, a significant interaction between hemisphere and load was obtained [($F(2,5) = 4.32$; $P = 0.044$), in which the left hemisphere]
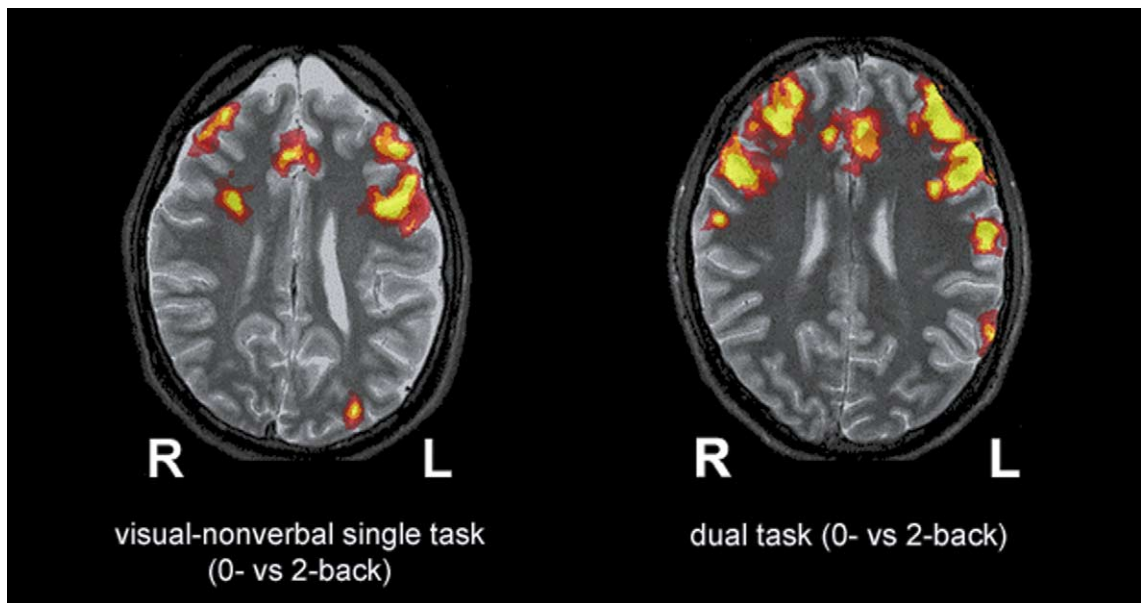
Fig. 5. Representative examples of individual activation patterns resulting from two selected task alternations. (A) Typical activation pattern in one subject for a dual task (0-back vs 2-back), including bilateral DLPFC, PRG, and CGa. (B) Typical activation pattern in another subject for the corresponding visual–nonverbal single task (0-back vs 2-back), including bilateral DLPFC, PRG, and CGa. For visualization from the whole depth of the sulci, z scores of slices (12 mm) were projected onto the center reference slice. This allows a representative display of the activation pattern. Clusters containing a z score of at least 5.0 (corresponding to a P < 0.01, with full Bonferroni correction for the whole 30-slice data volume) are included, but cluster extent is shown and color-coded down to a z score of 1.25 (corresponding to an uncorrected P < 0.01).

exhibited an increasing percentage signal change with augmented load, whereas the right hemisphere did not.

Differences in percentage signal change across input modality (auditory–verbal vs visual–nonverbal)

No VOI was obtained exhibiting a significant main effect of modality in the ANOVA hemisphere × modality on the percentage signal change ($0.01 \leq F(1,5) \leq 0.97$; $0.373 \leq P \leq 0.982$). Thus, it was possible to sum up the results of the realized contrasts in verbal and nonverbal single tasks (1-back to 3-back task with the 0-back task as control) for our further data analysis. Two VOIs exhibited a significant main effect of hemisphere. In both regions, in the inferior frontal VOI and in the temporal VOI, the mean activation was stronger in the left hemisphere than in the right hemisphere (inferior frontal: $F(1,5) = 49.16$; $P = 0.001$; temporal: $F(1,5) = 10.16$; $P = 0.024$).

Discussion

Summary of main results with reference to activations in the DLPFC

When subjects perform single tasks as well as dual tasks at different levels of difficulty, comparable activation patterns for both conditions seem to emerge in the DLPFC, indicating that both single and dual tasks enhance activation with increasing load in that region. Thus, it appears that

there are specific cortical areas, mainly prefrontal, which are critical for load-dependent processing, regardless of whether a task is performed as a single task or concurrently with a secondary task.

Hypothesis I: activation patterns in the DLPFC and behavioral performance resulting from the single tasks

With reference to our initial hypothesis concerning the single tasks, the expected relationship between activation in PFC and WM load was found to yield a monotous increase, although not with a strictly linear proportionality: as hypothesized, the smallest activation occurred under the 1-back condition and the strongest under the 3-back condition (see Fig. 3). But although the linear trend was significant, this relationship was most probably based on the significant increase from the 2-back to the 3-back condition. Additionally, the signal change was unexpectedly small under the 2-back condition and even negative under the 1-back condition (see Fig. 3). Thus, even though our data showed a monotonous increase in activation in the DLPFC, we failed to find substantial signal changes in the *n*-back single task at lower levels of load. In part, this is concordant with the literature (e.g., Braver et al., 1997; Callicott et al., 1999), where prominent activation in other regions, but little activation in the DLPFC was found in low-level single WM tasks, and especially in single 1-back tasks (Callicott et al., 1999, where a relevant increase in DLPFC activation is seen only under the 2-back condition). We explain these results

terms of the chosen criterion level of performance (at least 75% accuracy in the 2-back single task) in order to obtain a certain level of accuracy under the dual 1- and -back conditions, which might have led to that pattern. The selection of high-performing subjects could have resulted in the possibility that they were not challenged enough in these relatively simple 1- and 2-back tasks, suggesting that in this case there was not sufficient demand on the WM networks. The behavioral performance confirms the observed signal changes: the accuracy was very high and comparable under both the 1- and the 2-back conditions and only decreased under the 3-back task (see Fig. 2), indicating that the first two tasks were very easy to perform for our subjects indeed. The 0-back condition used as control task might also have contributed to the low activation patterns under the 1-and -back conditions: all three tasks were probably too similar and too easy to execute for our high-performing subjects and therefore did not yield sufficient signal changes.

Alternatively, the chosen VOI-based methodology for MRI data analysis could have contributed to the difficulty of detecting substantial DLPFC activation changes in those simple tasks, where signal changes are expected to be constrained to a relatively small volume, because the chosen VOIs were relatively large. However, the observed signal change under the dual 1-back condition, which was also expected to be of small size, was substantial and therefore speaks against a failure of detecting signal changes due to the chosen methodology.

Hypothesis II: activation patterns in the DLPFC and behavioral performance resulting from the dual tasks

Since single and dual tasks evoked comparable activation patterns, the hypothesis concerning the dual tasks could not be confirmed, given that we could not provide clear evidence for an attenuation or even just saturation of PFC activation under the dual-task condition even in the most difficult task (dual 3-back); rather, activation still increased (see Fig. 3) despite behavioral performance with an error rate corresponding to random selection. Thus, the assumption made by D'Esposito (2001) that prefrontal activation possibly decreases in the face of extreme processing demands, i.e., due to capacity limits of the CES, could not be supported. Instead, our results suggest that increased difficulty in dual tasks leads to a stronger activation in the PFC even if the processing demands are excessive. However, the increase in the dual tasks tended to be smaller than the increase in the single tasks, thus supplying some kind of evidence for a beginning saturation in the BOLD response. But still, the interaction between single- and dual-task activation was not significant and, additionally, the increase in signal change between the 2- and the 3-back tasks was also significant.

A possible explanation for the continuative increase in activation could be that memory load was not increased

limit of performance, i.e., that their processing capacity was not exceeded. Yet, taking the behavioral data into account, this argument would not apply, since performance dropped to chance level for all the subjects during the dual 3-back condition. In contrast to the activation patterns, which were the same for single and dual tasks, there was a significant difference in the behavioral performance, i.e., the subjects produced longer RTs and more errors in the dual tasks compared to the single tasks. Furthermore, subjective rating concerning the demands for the dual 3-back condition revealed that each subject experienced this condition as extremely difficult; hence, it can be concluded that the demands were excessive indeed. In summary, the DLPFC activation did not yet show saturation at a level of difficulty where the behavioral accuracy was already at chance level, as judged from the error rate.

Therefore, we conclude the following: the activation and the accuracy do not decrease or saturate accordingly; rather, they seem to behave quite independently, suggesting that the observed signal changes did not only represent WM processes only, but in addition some kind of "mental effort" or "willful attention" (Frith and Dolan, 1996; Ingvar, 1994) in order to cope with the task demands, attributable to executive functioning subscribed to the PFC. Postinterviews with our subjects clearly indicated that they tried hard in order to succeed in the given tasks. Such a notion, i.e., the high motivation of the subjects, could also explain the similar increasing activation curves in parietal and precentral regions and could also be taken into account for the capacity-unconstrained activation patterns in those regions.

Alternatively, our subjects could be considered as having accomplished selectively only one task under the dual-task condition, trying to ignore the stimuli of the secondary task in order to minimize interference. Such a process, i.e., selectively responding to one task only, despite our explicit request to allocate attention equally to both tasks, would have been a comprehensible strategy in order to accomplish at least one of the tasks sufficiently and is also an often-ascribed process attributed to executive functioning subscribed to the PFC (Klingberg and Roland, 1997). Nevertheless, the high accuracy achieved under the dual 1-back and 2-back conditions speaks for a high probability that the subjects executed the task in the intended mode. Additionally, the reaction times as well as the accuracy under the 3-back condition would have been comparable to those of the 3-back single task if the subjects had paid attention to one task only, which was not the case; rather, in the 3-back dual task the RTs significantly exceeded that achieved in the corresponding single task, whereas accuracy was reliably smaller.

Another reason why we could not support the hypothesis about a possible attenuation in the face of excessive demand could lie in the fact that this hypothesis was inferred on the basis of results from different studies (D'Esposito et al., 1995; Goldberg et al., 1998), with different subjects, using

constructs. This speaks to the possibility that specific task properties and the associated task demands may play an important role in determining activation patterns. In particular, the task used by Goldberg et al. (1998) also involved appreciable amounts of cognitive reasoning (Wisconsin card sorting test), which might also put demands on overlapping regions of the DLPFC and, thus, interfere with WM.

Hypothesis III: comparison of the activation patterns in the summed single tasks with the activation in the corresponding dual tasks

When we evaluated single- and dual-task activations to test our third hypothesis, the predicted interaction between WM load and the summed activations in the single tasks, compared with the activation in the corresponding dual tasks, could be confirmed: under the most difficult condition (3-back), the sum of activation changes in these single tasks exceeded the activation changes resulting from the 3-back dual task, whereas under the simpler 1-back and the 2-back conditions, the summed single-task activations were similar to the activations in the corresponding dual task (see Fig. 4).

These results are in agreement with findings by Just et al. (2001), who reported similar activation patterns in the prefrontal areas for their summed single tasks compared to the activation in the dual task, where the dual tasks could be performed "without compromising accuracy," as in our 1-back and 2-back tasks. A direct comparison between single and dual *n*-back task with excessive behavioral demands resulting in degradation of accuracy like our dual 3-back task has not been assessed before to our knowledge. Also, corresponding to the relatively low DLPFC activation levels in our 1-back and 2-back tasks, the activation Just et al. (2001) found in the DLPFC "was minimal in both single- and dual-task conditions," so that "the comparison of signal intensities in the prefrontal areas could not be made because many participants failed to show reliable activation in those areas." In contrast, the sum of our single-task activations exceeded the dual-task activations under the 3-back condition, although only at the tendency level. If accepted for real, this result can be interpreted in accordance with Navon and Gopher (1979) or Klingberg and Roland (1997), stating that concurrent tasks interfere with each other if they depend on a common resource pool, i.e., if they demand activation of the same part of the cortex. Such an interference is indicated by increasing RT along with increasing error rate and, additionally, as was the case in our experiment, by the smaller activation during the dual task compared to the total of activation during the single tasks under the 3-back condition. These smaller activations in the dual tasks could represent the physiological homologue of the above-mentioned behavioral cost (increasing RT and error rate).

Other studies also indicate that the BOLD response is relatively smaller in certain cortical areas if a secondary task is performed concurrently with a primary task, if both depend on resources of the same cortical area (e.g., Vanderberghe et al., 1997, or Rees et al., 1997). Just et al. (2001) suggested that any observed underadditivity in the dual task could be explained with a certain biological constraint in the amount of activation that can be distributed to an area at a given time. This constraint could be another manifestation of a generally assumed limit of attention which can be allocated to tasks at one time (e.g., Broadbent, 1957; Kahneman, 1973), resulting most evidently in the decrement of performance if several demanding tasks are required to be performed simultaneously. As a physiological reflection, this limit of attention might result in the relatively smaller activation of certain cortical areas involved with these tasks.

Just et al. (2001) mention the possibility that any observed underadditivity in prefrontal areas could be attributed to the nonlinearity of the BOLD response. There is evidence that, at high levels of demand, a saturation of the BOLD response may occur, i.e., leading to the lesser measurable activation in the involved areas (Friston et al., 2000). In our experiment, the criterion of a highly demanding task has been reached, at least in the case of the dual 3-back condition. However, although a certain underadditivity was observed during the dual tasks in our experiment, indicating a smaller increase under the dual-task condition compared with the single-task condition, the activation still increased with incremental memory load, therefore speaking against a saturation based solely on the BOLD response. Moreover, the observed maximal signal change even under the 3-back condition (0.39%) is only a fraction of what we observe with identical methodology in the motor cortex during motor tasks (up to 2.33%, Nirkko et al., 2001). It seems unlikely that the BOLD response should be saturated at such a lower threshold in these almost neighboring regions of the DLPFC. We conclude that the observed underadditivity reflects a neuronal phenomenon, not a limitation of the vascular or physical/technical BOLD response.

Regions apart from the DLPFC responding to manipulations of memory load

Apart from the DLPFC there are a few regions that similarly show load-dependent signal change: bilateral precentral gyrus (BA 4), bilateral superior parietal lobule (BA 39/40), left superior and middle temporal gyri (BA 21/37), and, to a certain extent, inferior frontal cortex (BA 44/45) (see Fig. 3).

These regions were commonly activated as a function of memory load in most studies, which used the *n*-back task as WM paradigm and, regarding the premotor and inferior–frontal regions, the assumption has been previously made (e.g., Braver et al., 1997, Smith and Jonides, 1997, or Rypma et al., 1999) that these regions house anterior speech areas and, concerning WM, that premotor and supplementary motor regions in cooperation with Broca's area mediate maintenance processes, especially subvocal articulatory

bserved in these regions might presumably reflect the in-
rease in number of rehearsal items associated with the
ontinuous augmentation of WM load.

Parietal cortex did not only produce the strongest overall
gnal change, but also exhibited increased activation with
ugmented WM load which is in accordance with studies by
aulesu et al. (1993), Smith and Jonides (1997), or Salmon
al. (1996), suggesting that the parietal cortex is critical for
honological storage processes.

With regard to temporal regions we observed a load-
ependent activation pattern for the left temporal cortex,
hich, similar to parietal regions, could account for phono-
ogical storage processes. According to Smith and Jonides
1997) there is some evidence that inferotemporal regions in
onnection with posterior parietal areas might mediate stor-
ge and rehearsal for object information in addition to
erbal information. However, temporal activations observed
 our experiment were very small (see Table 1) but still
howed a significant left-lateralized, load-dependent signal
hange that speaks for the involvement of verbal and/or
bject storage processes.

Hence, there seems to be a network of cortical regions
ediating WM tasks, including inferior frontal, parietal,
nd temporal areas, supporting a WM model like the one
roposed by Baddeley (1986) consisting of different sub-
omponents responsible for different processes carried out
 specific cortical areas.

*ifferences in activation between input modalities within
e PFC*

WM processes in our experiment seem to induce activa-
on in specific prefrontal areas regardless of the input mo-
ality (auditory/visual) or the type of the stimulus material
verbal/nonverbal) held in WM, supporting the "process-
pecific" theory proposed by Petrides (1994) or Owen et al.
1996). Still, there is evidence for a certain type of "mate-
al-specific" processing in the PFC, specifically concerning
e VLPFC, where verbal processing, as well as processing
f objects, is more likely to be reflected as activations in the
eft hemisphere (Broca's area) (e.g. Smith et al., 1997;
onides et al., 1997), compared to spatial processing mainly
voking activations in homologous areas in the right. In our
xperiment, the left VLPFC was more activated under both
ingle-task conditions (shapes and consonants) than the
ght VLPFC, speaking for a lateralized stimulus-based pro-
essing mechanism.

One explanation for these results is that our subjects can
e considered as having used the same encoding, maintain-
g, or manipulation strategies across both stimulus types,
g., that subjects verbalized and rehearsed the abstract
hapes as they did the verbal material. Indeed, posttest
terviews revealed that all subjects tended to verbalize the
hapes despite our efforts to select material designed to be
fficult to verbalize. In that case, the processing mecha-
isms for nonverbal and verbal material were likely to be

the same, and left-lateralization of the VLPFC was less due
to the stimulus material, but rather to similar processing
mechanisms, which could also explain the similar activa-
tions in the auditory and the visual tasks in the analyzed
VOIs. Other, more posterior regions (i.e., occipital areas), in
which modality-specific differences could be expected,
were not explicitly explored. Under the dual-task condition,
however, both tasks apparently competed for the same pro-
cessing system, most probably for the phonological loop,
assumed to be responsible for verbal rehearsal. Such a
competition for resources might additionally have led to the
observed interferences between the two tasks.

Conclusion

In sum, our results show that single and dual tasks
similarly enhance activation in the DLPFC with increasing
load; therefore, the intended interaction between the mem-
ory load and the activation in single and in dual tasks could
not be observed. This interaction, however, was significant
when the sum of the activation in the single tasks was
compared with the activation in the corresponding dual task,
i.e., the increase in activation was smaller in the dual tasks
in comparison with the increase of activation in the summed
single tasks. Under the 3-back condition, the activation of
the sum of both single tasks exceeded the activation in the
dual task for not less than 42%. However, this finding could
be expected, since the effects concerning the increase in
activation resulting from single-task performance due to
augmented memory load apparently became more substan-
tial when the doubled activation of these tasks was taken as
reference for the activation in the dual tasks. Further inves-
tigations with such methods would have address the ques-
tion of which type of evaluation would make more sense,
i.e., either to choose an evaluation comparing single tasks
and dual tasks as independent measures or, rather, to com-
pare the activation in dual tasks with the sum of two single
tasks which, in reality, were executed independently. It must
be considered that, presumably, the performance of a single
task demands entirely different processes compared with the
processes involved in the performance of a dual task.

Our study provides some informative evidence that be-
havioral measures (i.e., accuracy) are not necessarily related
to activation in involved regions in a direct mode, since
activation still increased even as performance was at chance
level in the most difficult task. Task difficulty, as expressed
in task load, and the related mental effort to execute the
tasks seem to play a crucial role for the observed activation
patterns, mainly in a distributed network comprising the
DLPFC, the superior parietal lobule, and precentral regions.
We conclude, that this motivation factor probably plays the
main role in decreases at higher levels of load reported by
other authors (e.g., Goldberg et al., 1998), especially if the
subjects fail to execute the task appropriately anymore and,

anymore. But, of course, such factors should be controlled
for, e.g., by posttest interviews.

We suggest that the load-dependent activation changes
we observed did not exclusively represent WM processes
per se, but rather a more global attentional, somehow mo-
tivational network (Frith and Dolan, 1996; Ingvar, 1994)
related to strategic task processing. These processes may not
be related to the decrement of behavioral performance, but,
explaining our data, seem to rely on the same neural sub-
strates that mediate the executive component of WM.

Consequently, further studies will be needed to deter-
mine carefully how and under which conditions dual-task
processing affects activation in specific cortical areas, in
order to clarify the role of capacity-constrained regions in
the human brain, as well as to separate WM demands from
those needed in more global attentional networks. The
coregistration and evaluation of behavioral data are crucial
in that context, as psychologically relevant reference func-
tion in order to interpret activation data. Furthermore, more
studies are needed to clarify the question of how dual-task
processing is related to single-task processing, along with
the reasons for possible occurrences of any deviations in the
observed activation patterns between dual and single tasks.
We suggest that the direct comparison of parametrically
varied single tasks with analogously varied dual-task con-
ditions might be a fruitful way to succeed.

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